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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,870	08/29/2005	Masayoshi Shichiri	4439-4028	5652

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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
10/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/518,870	SHICHIRI ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *5-11 and 15-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,12-14 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5 sheets, 9/24/2007; 2 sheets, 12/21/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group II, claims 1-8, 12-22, and the specie rifampicin as the form of ansamycin antibiotic and malignant tumor as the form of angiogenesis in the reply filed on 7/28/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-24 are pending in the application. Claims 5-11, 15-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected withdrawn, there being no allowable generic or linking claim. Accordingly, claim 24 is newly added, claims 13-14 are amended, and no claims have been cancelled.

This application is the national stage entry of PCT/JP03/07813 filed 6/19/2003; and claims benefit of foreign priority document JAPAN 2002-181281 filed 6/21/2002 and further claims benefit of foreign priority document JAPAN 2003-118960 filed 4/23/2003; currently an English language translation of these foreign priority documents have not been filed.

Claims 1-4, 12-14 and 24 are currently under examination and the subject of this Office Action.

Information Disclosure Statement

The information disclosure statements filed 9/24/2007 and 12/21/2004 have been received. Documents with no publication date were not considered.

Specification

The disclosure is objected to because of the following informalities: priority documents are not listed on the first page of the instant specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 12-14 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of angiogenesis of retinal microvascular endothelial cells (see present example 6 in the specification) by administering rifampicin, does not reasonably provide enablement for the treatment of *other* tumor types by administering rifampicin. The specification does not enable any person skilled in the art to which it pertains or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In regard, the application disclosure and claims have been compared per the factors indicated in the decision In re Wands, 8 USPQ 2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;

2) the breadth of the claims;

3) the predictability or unpredictability of the art;

4) the amount of direction or guidance presented;

5) the presence or absence of working examples;

6) the quantity of experimentation necessary;

7) the state of the prior art; and,

8) the relative skill of those skilled in the art.

The relevant factors are addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation. The presently claimed

invention is directed to a method for treating a maligntant tumor, comprising providing a composition comprising an effective amount of the elected compound, rifampicin, for the treatment of cancer.

In particular, one skilled in the art could not practice the presently claimed subject matter without undue experimentation because the artisan would not accept on its face that the treatment of any tumor type could be effectively achieved by the administration of the elected compound, rifampicin. Based upon the state of the art, as discussed below, the artisan would have only accepted that the treatment of specific tumor types could be achieved with this compound, rifampicin, identified as having activity in treating such a tumor. As set forth in *In re Marzocchi et al.,* 169 USPQ 367 (CCPA 1971): "[A] [s]pecification disclosure which contains the teachings of manner and process of making and using the invention in terms corresponding to the scope to those used in describing and defining subject matter sought to be patented must be taken as in compliance with the enabling requirement of first paragraph of 35 U.S.C. 112 *unless there is reason to doubt the objective truth of statements contained therein which must be relied on for enabling Support;* assuming that sufficient reasons for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proofs indicating that teaching contained in the specification is truly enabling." (emphasis added)

The present claims circumscribe a method of treating any type of cancer by treatment with use of rifampicin. That is, in order to be enabled to practice the present invention, the skilled artisan would have to accept that by administering the presently claimed compound rifampicin, all cancers, including papilloma, teratoma, adenoma, cervical cancer or leukemia, known in the art could be treated. In light of the fact that the specification not only fails to provide the skilled artisan with any direction or guidance as to how the treatment of any angiogenesis type, aside from angiogenesis occurring in retinal microvascular endothelial cells, could actually be achieved using the claimed rifampicin, but also fails to direct the skilled artisan as to which other tumor types would be sensitive to this chemotherapeutic agent and how one would determine such sensitivity, and especially in light of the highly complex nature of tumors and

cancer in general, the specification, which lacks an objective showing of which other tumors could be effectively treated using the claimed rifampicin, is viewed as lacking an enabling disclosure of the entire scope of the claimed invention.

Here, the objective truth that any tumor type may be treated with the claimed rifampicin is doubted because, while the state of the art of cancer treatment is well developed with regard to the treatment of specific cancer types with specific chemotherapeutic regimens (see Cecil's Textbook of Medicine, pages 1060-1074), the state of the art with regard to treating all tumors using a single agent is grossly underdeveloped. In this regard, Cecil's Textbook of Medicine (2000) is cited. In particular, there is no known anticancer agent or combination of anticancer agents that is effective against treating all cancer types, nor is there any known anticancer agent or combination of agents that is effective against inhibiting the growth of any type of cancer cell. The Cecil reference clearly shows that for the various known cancer

types, there is not one specific chemotherapeutic agent or combination thereof that is effective at treating cancer or inhibiting the growth of cancer cells-for each and every type of cancer (see Table 198-5 at page 1065; Tables 198-6 and 198-7 at pages 1066; Table 198-8 at page 1068;.and Table 198-9 at page 1071).

Given that there was not known any specific agent or combination of agents effective to treat all known types of cancer, one of ordinary skill in the art would not accept on its fact Applicant's statement that such an objective could be achieved in any type of tumor using the presently claimed rifampicin compound without enabling a set of species representative of the full scope of cancers known in the art. The artisan would have required sufficient direction as to how, at minimum, a representative set of species of cancer could be effectively treated with the rifampicin and, further, how the artisan could have reasonably extrapolated such results to the larger and highly varied genus of tumors in general without requiring undue experimentation to determine what types of tumors would actually show sensitivity to the presently claimed rifampicin, such that the artisan would have been imbued with at least a reasonable

expectation of success in treating the cancer. Such success would not have been reasonable expected for all cancer types claimed given the highly complex and variable nature of all cancers known in the art and that Applicant has shown an example retinal microvascular endothelial cells. To the artisan, the concept of a single agent effect to treat two specific tumor types would not have been considered representative or suggestive of the same efficacy in the treatment of all known types of tumor in the absence of any evidence or reasoning to do so. Additionally, since the skilled artisan would have expected the interaction of a particular agent in the treatment of a particular disease state to be very specific and highly unpredictable absent a clear understanding of the structural and biochemical basis for the use of each agent, one of skill in the art would have no other recourse but undue experimentation to undertake extensive testing to determine which other tumor types would be amenable to treatment using the claimed rifampicin.

It is in this regard that Applicant is directed to the MPEP at §2164.08. All questions of enablement are evaluated against the claimed subject matter. Concerning the breadth of a claim relevant to enablement, the only relevant concern is whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. The determination of the propriety of a rejection based upon the scope of a claim relative to the scope of enablement involves the determination of how broad the claim is with respect to the disclosure and the determination of whether one skilled in the art is enabled to use the *entire scope* of the claimed invention without undue experimentation.

A conclusion of a lack of enablement must take into consideration the unpredictability in the art at the time of the invention and the direction or guidance provided by Applicant. The amount of guidance required to be present in the specification as originally filed is directly proportional to the amount of knowledge in the art as well as the unpredictability in the art. In other words, if little or nothing is known in the prior art about an aspect of the claimed invention and the art is unpredictable, the specification

needs more detail and guidance as to how to use the invention in order to be enabling. Please reference *In re Fisher,* 417 F.2d 833,839, 166 USPQ 18, 24 (CCPA 1970) and *Chiron Corp. v. Genentech lnc.,* 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004).

The enablement of the working examples provided in the specification is not disputed. However, they are not representative of the breadth of the presently claimed subject matter. Applicant's claims broadly claim the use of the rifampicin for use in treating *any cancer.* The fact that Applicant has exemplified the use of this compound in retinal microvascular endothelial cells does not address the high degree of variability in the art in terms of the pathophysiological differences among tumor types and their reactivity to different anticancer compounds. Applicant has also failed to provide any evidence, or describe any protocol, that addresses this variability in the art such that one of ordinary skill in the art would have been imbued with at least a reasonable expectation of success in treating any tumor with the claimed compound based on the direction provided in the present specification. While the lack of a working embodiment cannot be the sole factor in determining enablement, the absence of substantial evidence commensurate in scope with the presently claimed subject matter, in light of the unpredictable nature of the art and the direction that Applicant has presented, provides additional weight to the present conclusion of insufficient enablement in consideration of the *Wands* factors as a whole.

For example, the term "solid tumor" alone encompasses three distinctly different categories of tumors: (1) sarcomas, those that arise from connective or supporting tissues, such as bone or muscle; (2) carcinomas, those that arise from glandular tissues and epithelial cells; and (3) lymphomas, those that arise from the lymphoid organs, such as the .lymph nodes, spleen or thymus. Though each of these three types can be lumped under the umbrella category of "solid tumor", the distinct etiology and pathophysiological differences between these three categories of solid tumor would not have imbued the skilled artisan with a reasonable expectation of success in treating any one or more of these types of solid tumor when efficacy had only been demonstrated in a single cervical cell line.

In light of such, it is clear that one of ordinary skill in the art would be faced with the impermissible burden of undue experimentation in order to execute the entire scope of the subject matter presently claimed. The basis for the present rejection is not simply that experimentation would be required, since it is clear from the state of the pharmaceutical and chemical arts that experimentation in this particular art is not at all uncommon, but that the level of experimentation required in order to practice this aspect of the invention in the absence of any enabling direction by Applicant would be *undue.* Please reference *In re Angstadt,* 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976), which states, "The test of enablement is not whether any experimentation is necessary, but whether, *experimentation is necessary, it is undue."* (emphasis added) Given the high degree of unpredictability noted and recognized in the art with regard to the treatment of tumors, the state of the art clearly precludes the general extrapolation of the results seen in two tumor types to the larger and much more highly varied genus of tumors as a whole. In the absence of any direction or guidance presented by Applicant as to how such a therapeutic objective could be achieved without necessitating an undue level of experimentation, the present disclosure is viewed as lacking an enabling disclosure of the *entire scope* of the presently claimed subject matter.

In view of the discussion of each of the preceding seven factors, the level of skill in the art is high and is at least that of a medical doctor with several years of experience in the art. As the cited art and discussion of the above factors establish, practicing the claimed method in the manner disclosed by Applicant would not imbue the skilled artisan with a reasonable expectation that the use of the rifampicin would have necessarily had efficacy in the treatment of any cancer type. In order to actually achieve such a result, it is clear from the discussion above that the skilled artisan could not rely upon Applicant's disclosure as required by 35 U.S.C. 112, first paragraph, and would have no alternative recourse but the impermissible burden of undue experimentation in order to practice the full scope of the presently claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 12-14 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Demkow et al (Pneumonologia I Alergologia Polska, 1998, provided by Applicant, Examiner is further providing a English language translation).

Demkow et al rifampicin, the elected ansamycin antibiotic inhibits angiogenesis (please refer to pages 10-13 for specific working examples).

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614